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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/484,537	06/07/95	QUEEN C	11823-002630

020350 HM12/1104
TOWNSEND AND TOWNSEND AND CREW LLP
TWO EMBARCADERO CENTER
8TH FLOOR
SAN FRANCISCO CA 94111-3834

EXAMINER	
BURKE, J	
ART UNIT	**PAPER NUMBER**
1642	31

DATE MAILED: 11/04/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/484,537	Queen et al
Examiner	**Group Art Unit**
Julie E. Burke, (Reeves), Ph.D.	1642

☒ Responsive to communication(s) filed on *9 Aug 1999*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *111-126 and 131-144* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *111-126 and 131-144* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 111-126, 131-142 have been amended. Claims 143-144 have been added. Claims 111-126 and 131-144 are pending and under examination.

2. The text of those sections of Title 35, U.S.C. Code not included in this Office action can be found in a prior Office Action.

3. The following Office Action contains some NEW GROUNDS of rejection necessitated by amendment.

4. The following defect in the Oath/declaration has been newly identified.

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

> It does not clearly state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

The declaration/oath states "see attached" is written under the statement claiming benefit under 35 U.S.C. 120. A page is apparently attached to the Oath/Declaration, which merely

recites a list of US Serial numbers and filing dates, standing alone. The attachment is not signed or dated by the inventors and contains no language suggesting that this is the attachment is the one in which the Oath /Declaration refers. The attachment does not contain the 35 U.S.C. 120 language as required. It is suggested that anew oath/declaration be submitted.

Claim Rejections - 35 U.S.C. § 112

6. The rejection of Claims 114, 118, 120-121, 124-126, 131-135, 137, 142, wherein they depend upon any of the preceding claims stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention (affinity constants) is withdrawn in view of the amendment(s) to the claims.

7. The rejection of Claims 111-112, 115, 116, 139-142 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reciting at least 65% or 70% identical is withdrawn in view of the declaration of Dr. Vasquez and Dr. Queen and upon further reconsideration.

8. The rejection of Claims 111-112, 115, 116, 139-142 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for humanization procedures, does not reasonably provide enablement for humanization that results in a selected variable region framework which is at least 65% or 70% identical to the donor immunoglobulin variable region framework is made again and maintained for the reasons set forth in the previous Office Action.

a. The response set forth on pages 15-18, the amendments to the claims taken in view of the declaration of Dr. Vasquez and Dr. Queen has been considered carefully but is deemed not to be persuasive. The response argues that the amino acids tolerant of modification re the framework regions and that the claims have been amended to state that sequence identity is determined by aligning the framework sequences by Kabat numbering system. The response provides an example of the alignment of a large number of immunoglobulin sequences by Kabat numbering in the Exhibit 2, declaration of Dr. Queen. This declaration as been considered carefully but is deemed not to be persuasive because the Kabat alignment in exhibit 2 shows the alignment of various human immunoglobulin sequences. This exhibit is not commensurate in scope with the claimed invention. Humanized antibodies typically contain CDRs from an antibody produced in one species (such as a rodent) and the framework regions from a human antibody. Therefore tp practice the claimed method, one skilled in the art would need to align rodent sequences with human sequences. The alignment presented in the specification and in Exhibit 1 is sufficient to demonstrate alignment between that particular mouse/human framework regions. However, the specification, the response and the Declarations provide no evidence that other

human framework regions would align, without gaps, with mouse or other rodent or other species of antibodies, as broadly encompassed int the claims. Applicant is reminded that the claims define the subject matter of his invention and that the specification cannot be relied upon to read limitations into the claims. Arguments presented that rely on particular distinguishing features are not persuasive where those features are not recited in the claims.

b. Second, the specification fail to provide adequate written description for the amendments presented in the claims, in particular, that "the percentage sequence identity is determined by aligning amino acids in said frameworks by Kabat numbering" as set forth below in the new grounds of rejection. The specification teaches alignment by Kabat method to determine percent homology and not percent identity. Protein homology encompasses the ancestral relationship between evolutionarily conserved proteins and also encompassed conservative amino acid substitutions, such as substituting a positively charged residue such as lysine or arginine. In contrast, percent sequence identity requires that each amino acid either be identical and not merely evolutionarily conserved or conservatively substituted. The response fails to make a link between the language in the specification and the language in the claims. Thus it would require one skilled in the art undue experimentation to align the framework regions by Kabat numbering system in order to determine the percent sequence identity, for the reasons set forth in the previous Office Action.

9. The rejection of Claims 114, 118, 120-121, 123, 124-125 and claims 126, 131 132-137, 142 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons set forth in the previous Office Action as evidenced by Groves et al (Hybridoma, Vol 6(1) 71 1987), Jones et al, (Nature Vol 321 522-525 1986) and Reichmann et al, (Nature Vol 332, 325-327 1988) is withdrawn in view of arguments set forth on pages 19-21, the amendments to the claims and upon further consideration.

Claim Rejections - 35 U.S.C. § 102

10. The rejection of Claims 111 and 115 under 35 U.S.C. 102(b) as being anticipated by Reichmann et al (Nature, Vol 332, 325-327 1988), as evidenced by Cheetham (Prot Engineering Vol 2(3) 170-172, 1988, reference AM in Paper no 10) is withdrawn in view of the amendment(s) to the claims and in view of the arguments set forth on pages 20-21.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 111-112, 115-116, 139-144 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over independent claims 1 and 35 of U. S. Patent No 5,693,761 or independent claim 1 of US Patent No 5,530,101 or independent claims 1, 11, 14 and 16 of US Patent No 5,693,762. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims recite the same patent features of humanized antibodies, DNA encoding humanized antibodies and methods of making humanized antibodies wherein the sequence of the heavy or light chain variable region framework is at least 65% identical to the sequence of the donor immunoglobulin heavy or light chain variable region framework.

13. Claims 112 and 113 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,693,761, claim 3 of US patent 5,530,101 and claims 3 and 7 of US patent No 5,693,762. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims recite

the same patent features of binding antigen with an affinity constant of at least 10^7 and having no greater than four fold affinity of that of the donor immunoglobulin.

14. Claims 113-114, 117-123, 124-126, 131-138 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10, 11 and 37 of U.S. Patent No. 5,693,761 and claims 1-4 of US patent 5,585,089. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims recite the same patent feature of wherein each of the donor amino acids are adjacent to a CDR in the donor immunoglobulin sequence, are capable of interacting with amino acids in the CDRs or is typical at its position for human immunoglobulin sequences and the substituted amino acid in the acceptor is rare at its position for the human immunoglobulin sequences.

15. The response filed 8/9/99 fails to address the preceding double patenting rejections, thus the rejection re made again and maintained.

16. The following NEW GROUNDS of rejection have been necessitated by amendment.

17. Claims 111-113, 115-116, 139-144 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims have been amended to recite "wherein percentage sequence identity is determined by aligning amino acids in said frameworks

by Kabat numbering". The response states the support for this amendment is found on page 30 lines 16-18 and page 4 lines 17-20. These passages refer to percent homology and not percent identity. The term homology refers to a different measurement than percent identity. For example, homology may encompass the evolutionary relationship pf proteins or may refer to conservative amino acid substitutions, while the measurement of sequence identity requires that particular amino acid residues be identical to another. Applicant is required to either point to where the specification provides support for the phrase or to remove it from the claims.

18. Claims 111 and 143 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Newly amended claim 111 is indefinite for reciting "binds a predetermined antigen" because it is not clear by whom and under what criteria the antigen has been "predetermined". As written, it is impossible for one skilled in the art to determine the metes and bounds of the claims.

b. Newly added claim 143 appears to be missing text. Following the period, the claim recites "(III)" as though applicant had intended to include a third criteria.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Burke, nee Reeves, Ph.D., whose telephone number is (703) 308-7553. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

21. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

J. Burke

Julie E.Burke, nee Reeves, Ph.D.

Primary Examiner

(703) 308-7553

JULIE BURKE
PRIMARY EXAMINER